

Supplementary Information for

**The effect of standardized food intake on the association between BMI and <sup>1</sup>H-NMR metabolites**

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**Supplementary Figure S1** | Effect size of the association between BMI and metabolites in fasting status in this study and Würtz *et al.* (2014)<sup>1</sup>

**Supplementary Figure S2** | Effect size of the association between BMI and metabolites before and after the standardized liquid meal

**Supplementary Figure S3** | Effect size of the association between insulin and metabolites before and after the standardized liquid meal.

**Supplementary Figure S4** | Histogram of the time between consumption of the SLM and the collection of the non-fasted blood sample, in minutes.

**Supplementary Table S1** | Changes in metabolite levels after the standardized liquid meal

**Supplementary Table S2** | Effect size of the association between BMI and metabolites before and after the standardized liquid meal

**Supplementary Table S3** | Effect size of the association between BMI and metabolites in this study and study done by Würtz *et al.* (2014)<sup>1</sup>

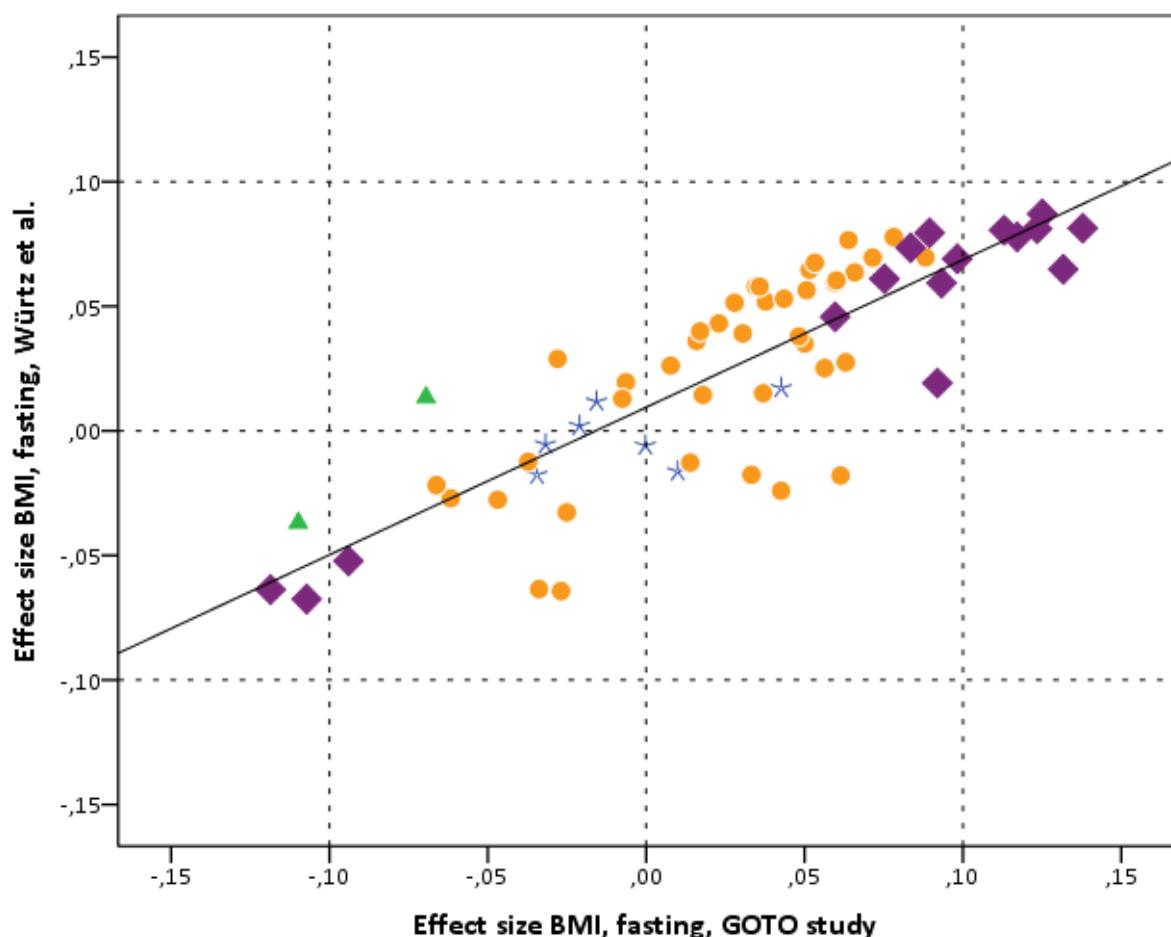
**Supplementary Table S4** | Interaction between SLM and BMI

**Supplementary Table S5** | Effect size of the association between diastolic blood pressure and metabolites before and after the standardized liquid meal

**Supplementary Table S6** | Effect size of the association between insulin and metabolites before and after the standardized liquid meal

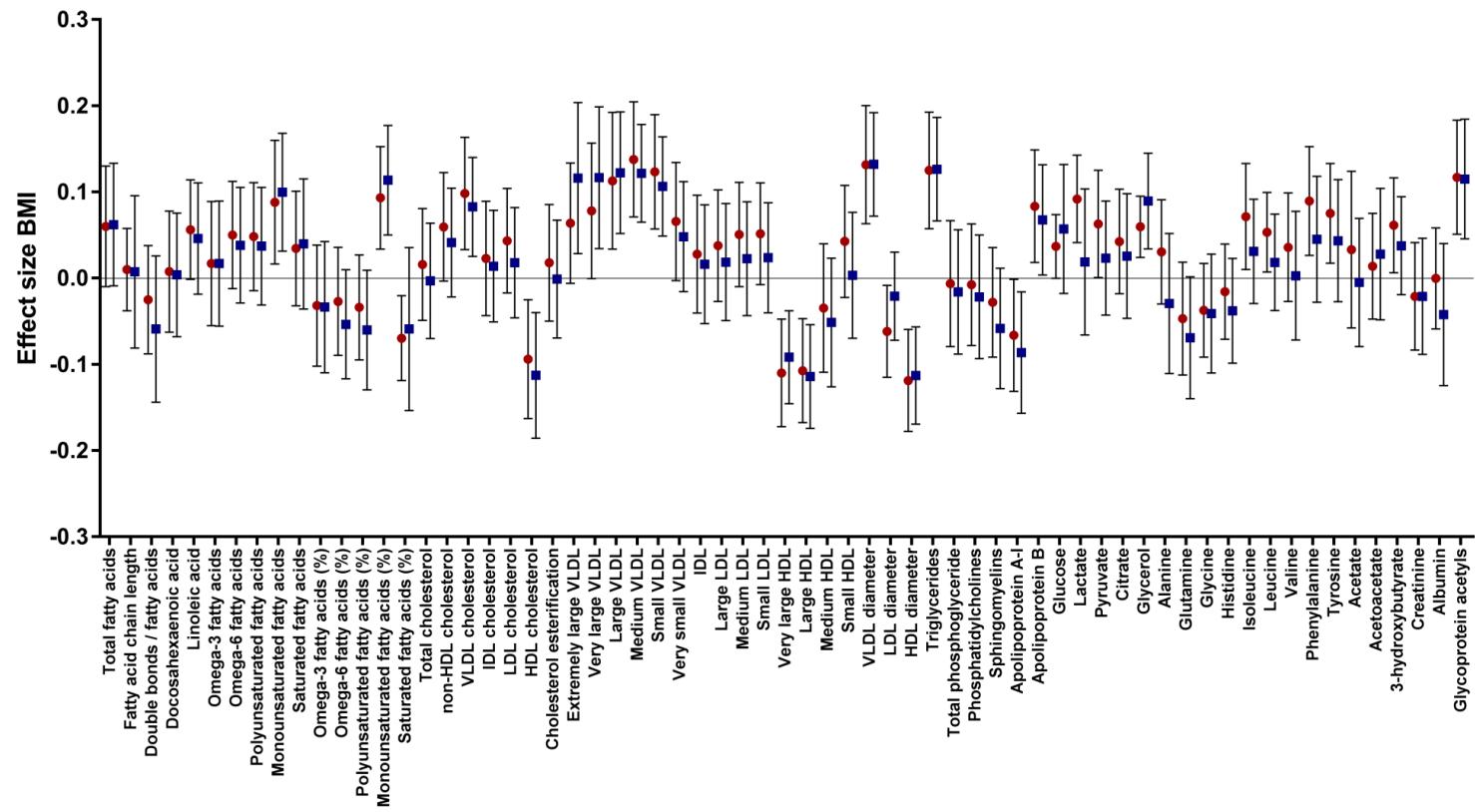
**Supplementary Table S7** | Nutritional content Nutridrink

**Supplementary Table S8** | Nutritional content amino acids Nutridrink



**Supplementary Figure S1** | Effect size of the association between BMI and metabolites in fasting status in this study and Würtz *et al.* (2014)<sup>1</sup>

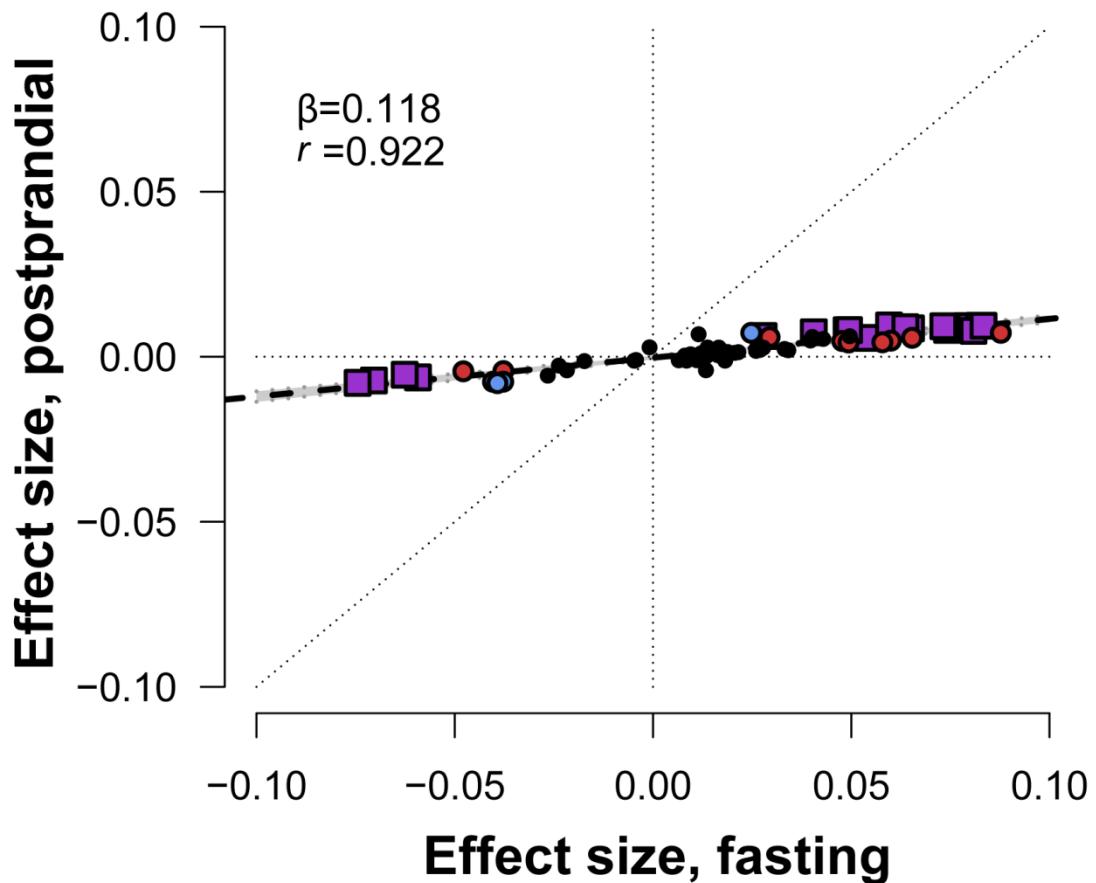
Effect sizes indicate the association magnitudes in units of 1-SD metabolite concentration per 1- $\text{kg}/\text{m}^2$  increment in BMI. Each dot represents a metabolite. Purple diamonds indicate the metabolite was significantly associated with BMI in this study and Würtz *et al.*; green triangle: only significant in this study; orange circles: only significant in the study of Würtz *et al.*; blue crosses: not significant in one of the studies



**Supplementary Figure S2 |** Effect size of the association between BMI and metabolites before and after the standardized liquid meal

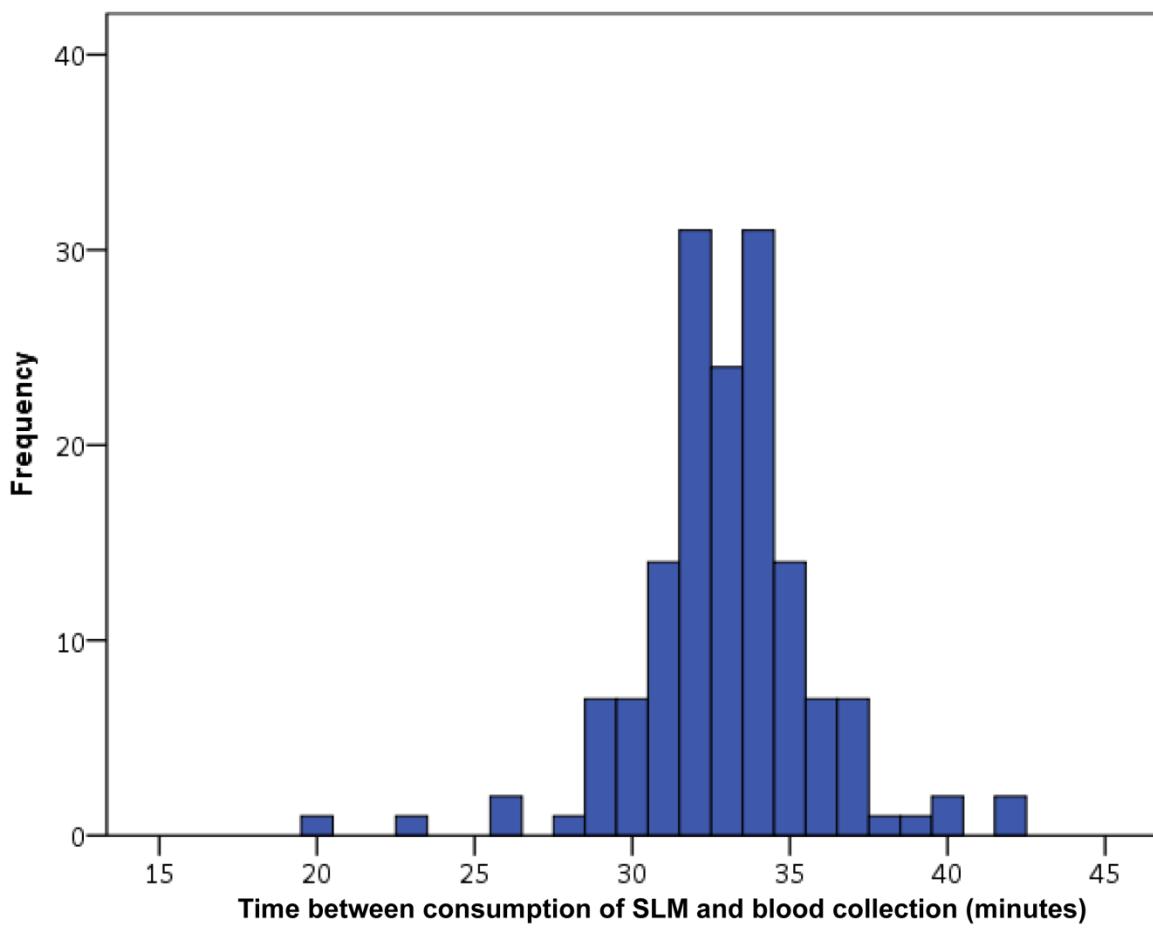
Effect sizes indicate the association magnitudes in units of 1-SD metabolite concentration per 1-kg/m<sup>2</sup> increment in BMI. Error bars indicate 95% confidence interval. Red circles indicate the effect size in fasting samples; blue squares indicate the effect size in postprandial samples. Double bonds/fatty acids: the number of double bonds in fatty acids. VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

# Insulin



**Supplementary Figure S3** | Effect size of the association between insulin and metabolites before and after the standardized liquid meal.

Effect sizes indicate the association magnitudes in units of 1-SD metabolite concentration per 1-SD metabolite concentration per 1-MU/L increment in insulin. Each dot represents a metabolite. Purple squares indicate the metabolite was significantly associated with BMI before and after the standardized liquid meal; red circles: only significant in fasting samples; blue circles: only significant in postprandial samples; black circles: not significant in fasting and postprandial samples



**Supplementary Figure S4 |** Histogram of the time between consumption of the SLM and the collection of the non-fasted blood sample, in minutes.

**Supplementary Table S1** | Changes in metabolite levels after the standardized liquid meal

	N	Change	P-value*	95% CI	
<b>Fatty acids</b>					
Total fatty acids	146	0.169	<b>2.05E-04</b>	0.080	0.259
Fatty acid chain length	146	0.409	<b>1.80E-04</b>	0.195	0.624
Double bonds / fatty acids	146	-0.070	0.262	-0.192	0.052
Docosahexaenoic acid	146	0.083	<b>0.001</b>	0.034	0.132
Linoleic acid	146	0.095	<b>0.006</b>	0.027	0.163
Omega-3 fatty acids	146	0.135	<b>4.38E-06</b>	0.077	0.192
Omega-6 fatty acids	146	0.092	<b>0.021</b>	0.014	0.170
Polyunsaturated fatty acids	146	0.104	<b>0.010</b>	0.025	0.183
Monounsaturated fatty acids	146	0.087	<b>0.031</b>	0.008	0.166
Saturated fatty acids	146	0.241	<b>8.53E-05</b>	0.121	0.361
<b>Fatty acids, relative to total fatty acids</b>					
Omega-3 fatty acids (%) <sup>†</sup>	146	0.016	0.493	-0.030	0.063
Omega-6 fatty acids (%) <sup>†</sup>	146	-0.169	<b>0.004</b>	-0.284	-0.054
Polyunsaturated fatty acids (%) <sup>†</sup>	146	-0.159	<b>0.009</b>	-0.277	-0.040
Monounsaturated fatty acids (%) <sup>†</sup>	146	-0.063	0.128	-0.144	0.018
Saturated fatty acids (%) <sup>†</sup>	146	0.256	<b>0.008</b>	0.066	0.447
<b>Cholesterol</b>					
Total cholesterol	153	0.114	<b>4.22E-04</b>	0.051	0.177
Non-HDL cholesterol	153	0.198	<b>2.11E-11</b>	0.140	0.256
VLDL cholesterol	153	0.477	<b>6.08E-35</b>	0.401	0.552
IDL cholesterol	153	0.301	<b>6.32E-20</b>	0.237	0.366
LDL cholesterol	153	-0.016	0.563	-0.069	0.037
HDL cholesterol	153	-0.216	<b>7.77E-19</b>	-0.264	-0.169
Cholesterol esterification	146	0.116	<b>3.75E-04</b>	0.052	0.180
<b>Lipoprotein lipid concentration</b>					
Extremely large VLDL	149	0.772	<b>3.26E-52</b>	0.673	0.872
Very large VLDL	148	0.538	<b>1.55E-31</b>	0.448	0.629
Large VLDL	150	0.232	<b>4.09E-08</b>	0.149	0.315
Medium VLDL	153	0.190	<b>3.36E-07</b>	0.117	0.263
Small VLDL	153	0.131	<b>9.75E-05</b>	0.065	0.197
Very small VLDL	153	0.270	<b>9.75E-14</b>	0.199	0.341
IDL	153	0.162	<b>3.07E-07</b>	0.100	0.224
Large LDL	153	0.000	0.988	-0.056	0.056
Medium LDL	153	-0.135	<b>1.22E-06</b>	-0.190	-0.081
Small LDL	153	-0.134	<b>3.93E-07</b>	-0.185	-0.082
Very large HDL	153	0.473	<b>3.71E-76</b>	0.423	0.523
Large HDL	148	-0.137	<b>4.33E-12</b>	-0.176	-0.098
Medium HDL	153	-0.599	<b>2.58E-43</b>	-0.684	-0.514
Small HDL	153	-0.829	<b>4.35E-54</b>	-0.934	-0.724

**Supplementary Table S1 (continued)** | Changes in metabolite levels after the standardized liquid meal

	N	Change	P-value*	95% CI	
<b>Lipoprotein particle size</b>					
VLDL diameter	153	0.235	<b>1.43E-08</b>	0.154	0.316
LDL diameter	153	0.653	<b>3.47E-32</b>	0.545	0.762
HDL diameter	153	0.254	<b>1.99E-47</b>	0.219	0.288
<b>Apolipoproteins and lipids</b>					
Triglycerides	153	-0.021	0.563	-0.091	0.050
Total phosphoglyceride	146	-0.104	<b>7.82E-03</b>	-0.181	-0.027
Phosphatidylcholines	146	-0.007	0.859	-0.085	0.071
Sphingomyelins	146	0.129	<b>4.58E-04</b>	0.057	0.202
Apolipoprotein A-I	153	-0.128	<b>2.53E-04</b>	-0.196	-0.059
Apolipoprotein B	153	0.185	<b>2.24E-09</b>	0.125	0.246
<b>Glycolysis related metabolites</b>					
Glucose	153	0.672	<b>7.44E-14</b>	0.496	0.848
Lactate	153	-0.489	<b>1.52E-05</b>	-0.711	-0.268
Pyruvate	151	0.035	0.681	-0.131	0.201
Citrate	153	-0.074	0.408	-0.251	0.102
Glycerol	151	-1.014	<b>4.46E-60</b>	-1.135	-0.892
<b>Amino acids</b>					
Alanine	151	0.567	<b>1.94E-19</b>	0.444	0.690
Glutamine	151	0.410	<b>2.51E-11</b>	0.289	0.530
Glycine	135	-0.468	<b>1.79E-11</b>	-0.604	-0.331
Histidine	153	-0.273	<b>0.00771</b>	-0.473	-0.072
Isoleucine	150	0.853	<b>1.9E-42</b>	0.731	0.976
Leucine	152	1.146	<b>3.15E-89</b>	1.034	1.258
Valine	151	0.506	<b>7.93E-11</b>	0.354	0.659
Phenylalanine	153	-0.554	<b>1.28E-11</b>	-0.714	-0.394
Tyrosine	153	-0.165	0.093	-0.358	0.027
<b>Ketone bodies</b>					
Acetate	153	-0.452	<b>1.62E-14</b>	-0.567	-0.336
Acetoacetate	153	-0.711	<b>6.66E-16</b>	-0.884	-0.538
3-hydroxybutyrate	151	0.227	<b>3.28E-05</b>	0.120	0.334
<b>Fluid balance</b>					
Creatinine	152	-0.394	<b>1.55E-10</b>	-0.515	-0.273
Albumin	153	-0.294	<b>0.001</b>	-0.466	-0.122
<b>Inflammation markers</b>					
Glycoprotein acetyls	153	0.389	<b>2.22E-16</b>	0.296	0.483

Changes are in units of 1-SD metabolite concentration

\* Bold p-values indicate significant associations after FDR correction

† % of total fatty acids

Double bonds/fatty acids: the number of double bonds in fatty acids. VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

**Supplementary Table S2** | Effect size of the association between BMI and metabolites before and after the standardized liquid meal

	N	B	fasting			postprandial		
			p-value*	95% CI	B	p-value*	95% CI	
<b>Fatty acids</b>								
Total fatty acids	146	0.060	0.091	-0.010	0.130	0.062	0.086	-0.009
Fatty acid chain length	146	0.010	0.679	-0.038	0.058	0.007	0.870	-0.081
Double bonds / fatty acids	146	-0.025	0.430	-0.088	0.038	-0.059	0.171	-0.144
Docosahexaenoic acid	146	0.008	0.828	-0.063	0.078	0.004	0.915	-0.068
Linoleic acid	146	0.056	0.055	-0.001	0.114	0.046	0.161	-0.019
Omega-3 fatty acids	146	0.017	0.640	-0.055	0.089	0.017	0.643	-0.056
Omega-6 fatty acids	146	0.050	0.114	-0.012	0.112	0.038	0.261	-0.029
Polyunsaturated fatty acids	146	0.048	0.130	-0.014	0.111	0.037	0.282	-0.031
Monounsaturated fatty acids	146	0.088	0.016	0.017	0.160	0.100	<b>0.005</b>	0.031
Saturated fatty acids	146	0.035	0.304	-0.032	0.101	0.040	0.298	-0.036
<b>Fatty acids, relative to total fatty acids</b>								
Omega-3 fatty acids (%) <sup>†</sup>	146	-0.032	0.371	-0.102	0.038	-0.034	0.384	-0.110
Omega-6 fatty acids (%) <sup>†</sup>	146	-0.027	0.396	-0.089	0.036	-0.054	0.096	-0.117
Polyunsaturated fatty acids (%) <sup>†</sup>	146	-0.034	0.273	-0.095	0.027	-0.060	0.089	-0.129
Monounsaturated fatty acids (%) <sup>†</sup>	146	0.093	<b>0.002</b>	0.034	0.153	0.114	<b>0.001</b>	0.050
Saturated fatty acids (%) <sup>†</sup>	146	-0.070	<b>0.006</b>	-0.119	-0.020	-0.059	0.218	-0.153
<b>Cholesterol</b>								
Total cholesterol	153	0.016	0.628	-0.049	0.081	-0.003	0.926	-0.070
Non-HDL cholesterol	153	0.060	0.064	-0.003	0.123	0.041	0.197	-0.022
VLDL cholesterol	153	0.098	<b>0.004</b>	0.033	0.163	0.083	<b>0.005</b>	0.025
IDL cholesterol	153	0.023	0.493	-0.043	0.089	0.014	0.670	-0.051
LDL cholesterol	153	0.044	0.158	-0.017	0.104	0.018	0.580	-0.046
HDL cholesterol	153	-0.094	<b>0.008</b>	-0.163	-0.025	-0.113	<b>0.003</b>	-0.186
Cholesterol esterification	146	0.018	0.600	-0.050	0.086	-0.001	0.976	-0.069

**Supplementary Table S2 (continued)** | Effect size of the association between BMI and metabolites before and after the standardized liquid meal

	N	B	p-value*	fasting		postprandial		
				95% CI	B	p-value*	95% CI	
<b>Lipoprotein lipid concentration</b>								
Extremely large VLDL	149	0.064	0.073	-0.006	0.134	0.116	<b>0.010</b>	0.028
Very large VLDL	148	0.078	0.051	0.000	0.157	0.117	<b>0.006</b>	0.034
Large VLDL	150	0.113	<b>0.006</b>	0.034	0.192	0.122	<b>0.001</b>	0.052
Medium VLDL	153	0.138	<b>8.81E-05</b>	0.071	0.205	0.122	<b>4.73E-05</b>	0.065
Small VLDL	153	0.123	<b>3.59E-04</b>	0.057	0.190	0.107	<b>3.90E-04</b>	0.049
Very small VLDL	153	0.066	0.059	-0.003	0.134	0.048	0.138	-0.016
IDL	153	0.028	0.420	-0.040	0.096	0.016	0.643	-0.053
Large LDL	153	0.038	0.249	-0.027	0.102	0.019	0.588	-0.049
Medium LDL	153	0.051	0.099	-0.010	0.111	0.023	0.499	-0.043
Small LDL	153	0.052	0.086	-0.007	0.111	0.024	0.463	-0.040
Very large HDL	153	-0.110	<b>0.001</b>	-0.172	-0.047	-0.092	<b>0.001</b>	-0.146
Large HDL	148	-0.107	<b>0.001</b>	-0.168	-0.047	-0.114	<b>2.95E-04</b>	-0.174
Medium HDL	153	-0.034	0.361	-0.109	0.040	-0.051	0.176	-0.126
Small HDL	153	0.043	0.196	-0.022	0.108	0.003	0.928	-0.070
<b>Lipoprotein particle size</b>								
VLDL diameter	153	0.132	<b>2.43E-04</b>	0.063	0.200	0.132	<b>3.16E-05</b>	0.072
LDL diameter	153	-0.062	0.024	-0.115	-0.008	-0.021	0.419	-0.072
HDL diameter	153	-0.119	<b>1.35E-04</b>	-0.178	-0.059	-0.113	<b>1.40E-04</b>	-0.169
<b>Apolipoproteins and lipids</b>								
Triglycerides	153	0.125	<b>3.89E-04</b>	0.058	0.193	0.126	<b>6.58E-05</b>	0.066
Total phosphoglyceride	146	-0.006	0.862	-0.079	0.067	-0.016	0.663	-0.088
Phosphatidylcholines	146	-0.008	0.833	-0.078	0.063	-0.022	0.549	-0.093
Sphingomyelins	146	-0.028	0.383	-0.092	0.035	-0.058	0.100	-0.128
Apolipoprotein A-I	153	-0.066	0.046	-0.131	-0.001	-0.086	0.017	-0.157
Apolipoprotein B	153	0.083	<b>0.013</b>	0.018	0.149	0.068	0.038	0.004

**Supplementary Table S2 (continued)** | Effect size of the association between BMI and metabolites before and after the standardized liquid meal

	N	B	p-value*	fasting		postprandial		
				95% CI	B	p-value*	95% CI	
<b>Glycolysis related metabolites</b>								
Glucose	153	0.037	0.050	0.000	0.074	0.057	0.133	-0.018
Lactate	153	0.092	<b>0.001</b>	0.041	0.143	0.019	0.659	-0.066
Pyruvate	151	0.063	0.047	0.001	0.125	0.023	0.485	-0.043
Citrate	153	0.043	0.167	-0.018	0.103	0.026	0.484	-0.047
Glycerol	151	0.060	<b>0.001</b>	0.024	0.095	0.089	<b>0.002</b>	0.034
<b>Amino acids</b>								
Alanine	151	0.030	0.319	-0.030	0.091	-0.029	0.475	-0.110
Glutamine	151	-0.047	0.159	-0.112	0.019	-0.069	0.056	-0.140
Glycine	135	-0.037	0.177	-0.092	0.017	-0.041	0.240	-0.110
Histidine	153	-0.016	0.575	-0.071	0.040	-0.038	0.219	-0.099
Isoleucine	150	0.072	0.023	0.010	0.133	0.031	0.308	-0.029
Leucine	152	0.053	0.024	0.007	0.099	0.018	0.518	-0.038
Valine	151	0.036	0.262	-0.027	0.099	0.003	0.939	-0.072
Phenylalanine	153	0.089	<b>0.006</b>	0.026	0.153	0.045	0.224	-0.028
Tyrosine	153	0.075	<b>0.011</b>	0.017	0.133	0.044	0.226	-0.027
<b>Ketone bodies</b>								
Acetate	153	0.033	0.470	-0.058	0.124	-0.005	0.896	-0.079
Acetoacetate	153	0.014	0.654	-0.047	0.075	0.028	0.469	-0.048
3-hydroxybutyrate	151	0.061	0.029	0.006	0.116	0.038	0.191	-0.019
<b>Fluid balance</b>								
Creatinine	152	-0.021	0.504	-0.083	0.041	-0.021	0.536	-0.088
Albumin	153	0.000	0.993	-0.059	0.058	-0.042	0.312	-0.125
<b>Inflammation markers</b>								
Glycoprotein acetyls	153	0.117	<b>0.001</b>	0.051	0.183	0.115	<b>0.001</b>	0.046
								0.184

Effect sizes indicate the association magnitudes in units of 1-SD metabolite concentration per 1-kg/m<sup>2</sup> increment in BMI

\* Bold p-values indicate significant associations after FDR correction. <sup>†</sup> % of total fatty acids

Double bonds/fatty acids: the number of double bonds in fatty acids. VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

**Supplementary Table S3** | Effect size of the association between BMI and metabolites in this study and study done by Würtz *et al.* (2014)<sup>1</sup>

	GOTO			Würtz		
	B	SE	p-value	B	SE	p-value
<b>Fatty acids</b>						
Total fatty acids	0.060	0.035	0.091	0.060	0.003	<b>1.74E-71</b>
Fatty acid chain length	0.010	0.024	0.679	-0.016	0.006	6.70E-03
Double bonds / fatty acids	-0.025	0.032	0.430	-0.033	0.004	<b>8.51E-17</b>
Docosahexaenoic acid	0.008	0.035	0.828	0.026	0.005	<b>3.90E-07</b>
Linoleic acid	0.056	0.029	0.055	0.025	0.004	<b>3.24E-10</b>
Omega-3 fatty acids	0.017	0.036	0.640	0.040	0.006	<b>9.50E-13</b>
Omega-6 fatty acids	0.050	0.031	0.114	0.035	0.005	<b>5.36E-14</b>
Polyunsaturated fatty acids	0.048	0.032	0.130	0.038	0.005	<b>5.83E-15</b>
Monounsaturated fatty acids	0.088	0.036	0.016	0.070	0.003	<b>2.37E-145</b>
Saturated fatty acids	0.035	0.033	0.304	0.058	0.003	<b>2.52E-102</b>
<b>Fatty acids, relative to total fatty acids</b>						
Omega-3 fatty acids (%) <sup>†</sup>	-0.032	0.035	0.371	-0.005	0.004	0.135
Omega-6 fatty acids (%) <sup>†</sup>	-0.027	0.032	0.396	-0.064	0.003	<b>1.03E-117</b>
Polyunsaturated fatty acids (%) <sup>†</sup>	-0.034	0.031	0.273	-0.064	0.004	<b>1.13E-71</b>
Monounsaturated fatty acids (%) <sup>†</sup>	0.093	0.030	<b>0.002</b>	0.059	0.002	<b>1.88E-159</b>
Saturated fatty acids (%) <sup>†</sup>	-0.070	0.025	<b>0.006</b>	0.013	0.004	8.95E-04
<b>Cholesterol</b>						
Total cholesterol	0.016	0.033	0.628	0.036	0.003	<b>2.58E-30</b>
non HDL cholesterol	0.060	0.032	0.064	0.060	0.003	<b>3.07E-107</b>
VLDL cholesterol	0.098	0.033	<b>0.004</b>	0.069	0.003	<b>8.41E-110</b>
IDL cholesterol	0.023	0.033	0.493	0.043	0.003	<b>7.44E-49</b>
LDL cholesterol	0.044	0.031	0.158	0.053	0.002	<b>1.47E-116</b>
HDL cholesterol	-0.094	0.035	<b>0.008</b>	-0.052	0.002	<b>1.72E-133</b>
Cholesterol esterification	0.018	0.034	0.600	0.014	0.003	<b>2.17E-05</b>
<b>Lipoprotein lipid concentration</b>						
Extremely large VLDL	0.064	0.035	0.073	0.077	0.002	<b>8.74E-287</b>
Very large VLDL	0.078	0.040	0.051	0.078	0.002	<b>2.43E-231</b>
Large VLDL	0.113	0.040	<b>0.006</b>	0.081	0.002	<b>3.66E-294</b>
Medium VLDL	0.138	0.034	<b>8.81E-05</b>	0.081	0.003	<b>4.68E-163</b>
Small VLDL	0.123	0.033	<b>3.59E-04</b>	0.081	0.004	<b>2.95E-114</b>
Very small VLDL	0.066	0.034	0.059	0.064	0.002	<b>1.15E-188</b>
IDL	0.028	0.034	0.420	0.051	0.003	<b>1.24E-90</b>
Large LDL	0.038	0.033	0.249	0.052	0.002	<b>6.12E-120</b>
Medium LDL	0.051	0.030	0.099	0.056	0.002	<b>4.25E-149</b>
Small LDL	0.052	0.030	0.086	0.065	0.002	<b>2.20E-202</b>
Very large HDL	-0.110	0.031	<b>0.001</b>	-0.037	0.013	5.49E-03
Large HDL	-0.107	0.030	<b>0.001</b>	-0.068	0.002	<b>3.93E-185</b>
Medium HDL	-0.034	0.038	0.361	-0.018	0.010	0.079
Small HDL	0.043	0.033	0.196	0.017	0.012	0.151

**Supplementary Table S3 (continued)** | Effect size of the association between BMI and metabolites in this study and study done by Würtz *et al.* (2014)<sup>1</sup>

	GOTO			Würtz		
	B	SE	p-value	B	SE	p-value
<b>Lipoprotein particle size</b>						
VLDL diameter	0.132	0.035	<b>2.43E-04</b>	0.065	0.002	<b>3.74E-206</b>
LDL diameter	-0.062	0.027	0.024	-0.027	0.003	<b>2.38E-21</b>
HDL diameter	-0.119	0.030	<b>1.35E-04</b>	-0.064	0.009	<b>1.33E-11</b>
<b>Apolipoproteins and lipids</b>						
Triglycerides	0.125	0.034	<b>3.89E-04</b>	0.087	0.002	<b>0</b>
Total phosphoglyceride	-0.006	0.037	0.862	0.020	0.003	<b>5.14E-12</b>
Phosphatidylcholines	-0.008	0.036	0.833	0.013	0.003	<b>2.54E-06</b>
Sphingomyelins	-0.028	0.032	0.383	0.029	0.003	<b>3.03E-30</b>
Apolipoprotein A-I	-0.066	0.033	0.046	-0.022	0.003	<b>2.27E-14</b>
Apolipoprotein B	0.083	0.033	<b>0.013</b>	0.073	0.003	<b>3.68E-100</b>
<b>Glycolysis related metabolites</b>						
Glucose	0.037	0.019	0.050	0.015	0.004	<b>1.97E-05</b>
Lactate	0.092	0.026	<b>0.001</b>	0.019	0.003	<b>2.59E-10</b>
Pyruvate	0.063	0.031	0.047	0.028	0.005	<b>2.17E-08</b>
Citrate	0.043	0.031	0.167	-0.024	0.006	<b>2.32E-05</b>
Glycerol	0.060	0.018	<b>0.001</b>	0.046	0.007	<b>5.88E-11</b>
<b>Amino acids</b>						
Alanine	0.030	0.030	0.319	0.039	0.004	<b>1.06E-24</b>
Glutamine	-0.047	0.033	0.159	-0.028	0.005	<b>1.08E-07</b>
Glycine	-0.037	0.027	0.177	-0.012	0.004	<b>5.38E-04</b>
Histidine	-0.016	0.028	0.575	0.012	0.007	0.100
Isoleucine	0.072	0.031	0.023	0.070	0.003	<b>1.92E-105</b>
Leucine	0.053	0.023	0.024	0.067	0.002	<b>7.12E-249</b>
Valine	0.036	0.032	0.262	0.058	0.002	<b>3.70E-164</b>
Phenylalanine	0.089	0.032	<b>0.006</b>	0.079	0.002	<b>2.00E-292</b>
Tyrosine	0.075	0.029	<b>0.011</b>	0.061	0.004	<b>1.12E-60</b>
<b>Ketone bodies</b>						
Acetate	0.033	0.046	0.470	-0.018	0.002	<b>1.92E-14</b>
Acetoacetate	0.014	0.031	0.654	-0.013	0.002	<b>3.02E-08</b>
3-hydroxybutyrate	0.061	0.028	0.029	-0.018	0.002	<b>5.20E-15</b>
<b>Fluid balance</b>						
Creatinine	-0.021	0.031	0.504	0.002	0.007	0.776
Albumin	0.000	0.030	0.993	-0.006	0.005	0.196
<b>Inflammation markers</b>						
Glycoprotein acetyls	0.117	0.033	<b>0.001</b>	0.078	0.005	<b>4.67E-53</b>

Effect sizes indicate the association magnitudes in units of 1-SD metabolite concentration per 1-kg/m<sup>2</sup> increment in BMI

\* Bold p-values indicate significant associations after FDR correction. # Bold p-values indicate significant associations after Bonferroni correction. † % of total fatty acids

Double bonds/fatty acids: the number of double bonds in fatty acids. VLDL. very low density lipoprotein; IDL. intermediate density lipoprotein; LDL. low density lipoprotein; HDL. high density lipoprotein.

**Supplementary Table S4** | Interaction between SLM and BMI

	BMI					SLM x BMI					SLM				
	N	B	p-value*	95% CI		B	p-value*	95% CI		B	p-value*	95% CI			
<b>Fatty acids</b>															
Total fatty acids	146	0.060	0.089	-0.009	0.130	0.002	0.919	-0.034	0.037	0.121	0.808	-0.861	1.103		
Fatty acid chain length	146	0.021	0.385	-0.027	0.070	-0.026	0.631	-0.131	0.080	1.099	0.453	-1.794	3.992		
Double bonds / fatty acids	146	-0.030	0.343	-0.092	0.032	-0.024	0.454	-0.088	0.040	0.581	0.513	-1.178	2.340		
Docosahexaenoic acid	146	0.008	0.828	-0.062	0.078	-0.004	0.716	-0.024	0.017	0.184	0.519	-0.381	0.749		
Linoleic acid	146	0.055	0.060	-0.002	0.113	-0.008	0.591	-0.036	0.021	0.305	0.442	-0.479	1.089		
Omega-3 fatty acids	146	0.015	0.671	-0.056	0.087	0.003	0.802	-0.022	0.029	0.048	0.891	-0.645	0.740		
Omega-6 fatty acids	146	0.047	0.135	-0.015	0.109	-0.006	0.708	-0.039	0.026	0.258	0.566	-0.630	1.145		
Polyunsaturated fatty acids	146	0.045	0.154	-0.017	0.108	-0.005	0.748	-0.038	0.028	0.248	0.585	-0.650	1.146		
Monounsaturated fatty acids	146	0.086	0.018	0.015	0.157	0.015	0.312	-0.015	0.046	-0.329	0.432	-1.159	0.500		
Saturated fatty acids	146	0.039	0.249	-0.027	0.105	-0.003	0.920	-0.056	0.050	0.314	0.674	-1.161	1.788		
<b>Fatty acids, relative to total fatty acids</b>															
Omega-3 fatty acids (%) <sup>†</sup>	146	-0.034	0.339	-0.104	0.036	0.002	0.853	-0.023	0.028	-0.049	0.891	-0.754	0.656		
Omega-6 fatty acids (%) <sup>†</sup>	146	-0.033	0.301	-0.095	0.030	-0.015	0.615	-0.075	0.045	0.240	0.773	-1.410	1.890		
Polyunsaturated fatty acids (%) <sup>†</sup>	146	-0.040	0.195	-0.100	0.021	-0.014	0.647	-0.077	0.048	0.229	0.792	-1.490	1.947		
Monounsaturated fatty acids (%) <sup>†</sup>	146	0.089	<b>0.004</b>	0.030	0.148	0.029	0.058	-0.001	0.058	-0.834	0.044	-1.647	-0.022		
Saturated fatty acids (%) <sup>†</sup>	146	-0.057	0.024	-0.107	-0.008	-0.014	0.770	-0.106	0.078	0.622	0.628	-1.917	3.161		
<b>Cholesterol</b>															
Total cholesterol	153	0.015	0.647	-0.050	0.080	-0.017	0.194	-0.044	0.009	0.579	0.107	-0.128	1.286		
non-HDL cholesterol	153	0.058	0.070	-0.005	0.121	-0.015	0.211	-0.039	0.009	0.600	0.064	-0.037	1.237		
VLDL cholesterol	153	0.095	<b>0.004</b>	0.030	0.159	-0.009	0.580	-0.040	0.022	0.711	0.105	-0.152	1.575		
IDL cholesterol	153	0.022	0.505	-0.044	0.089	-0.008	0.569	-0.036	0.020	0.516	0.173	-0.231	1.262		
LDL cholesterol	153	0.043	0.163	-0.018	0.103	-0.024	0.032	-0.045	-0.002	0.621	0.035	0.044	1.199		
HDL cholesterol	153	-0.093	<b>0.009</b>	-0.162	-0.024	-0.021	0.021	-0.039	-0.003	0.345	0.163	-0.142	0.833		
Cholesterol esterification	146	0.017	0.627	-0.051	0.084	-0.016	0.226	-0.043	0.010	0.556	0.131	-0.168	1.280		

Supplementary Table S4 (continued) | Interaction between SLM and BMI

	BMI					BMI x SLM					SLM				
	N	B	p-value*	95% CI		B	p-value*	95% CI		B	p-value*	95% CI			
<b>Lipoprotein lipid concentration</b>															
Extremely large VLDL	149	0.062	0.080	-0.008	0.132	0.056	0.006	0.016	0.096	-0.741	0.176	-1.820	0.338		
Very large VLDL	148	0.076	0.054	-0.001	0.153	0.043	0.010	0.010	0.075	-0.613	0.174	-1.501	0.275		
Large VLDL	150	0.110	<b>0.006</b>	0.032	0.188	0.015	0.290	-0.013	0.044	-0.184	0.649	-0.982	0.615		
Medium VLDL	153	0.134	<b>1.21E-04</b>	0.067	0.200	-0.008	0.579	-0.035	0.020	0.396	0.297	-0.355	1.148		
Small VLDL	153	0.119	<b>4.96E-04</b>	0.054	0.185	-0.008	0.507	-0.033	0.016	0.354	0.300	-0.321	1.029		
Very small VLDL	153	0.063	0.069	-0.005	0.132	-0.013	0.402	-0.043	0.017	0.613	0.141	-0.208	1.434		
IDL	153	0.027	0.439	-0.042	0.095	-0.009	0.477	-0.036	0.017	0.417	0.245	-0.291	1.124		
Large LDL	153	0.036	0.263	-0.028	0.101	-0.017	0.155	-0.039	0.006	0.444	0.154	-0.170	1.058		
Medium LDL	153	0.049	0.103	-0.010	0.109	-0.026	0.030	-0.049	-0.002	0.554	0.077	-0.062	1.171		
Small LDL	153	0.051	0.088	-0.008	0.109	-0.026	0.020	-0.048	-0.004	0.563	0.055	-0.012	1.138		
Very large HDL	153	-0.109	<b>0.001</b>	-0.171	-0.047	0.016	0.184	-0.008	0.039	0.047	0.883	-0.591	0.686		
Large HDL	148	-0.107	<b>0.001</b>	-0.168	-0.046	-0.007	0.344	-0.022	0.008	0.058	0.782	-0.358	0.474		
Medium HDL	153	-0.035	0.362	-0.109	0.040	-0.017	0.326	-0.050	0.017	-0.151	0.745	-1.072	0.770		
Small HDL	153	0.045	0.168	-0.019	0.110	-0.045	0.028	-0.084	-0.005	0.369	0.504	-0.724	1.463		
<b>Lipoprotein particle size</b>															
VLDL diameter	153	0.128	<b>2.83E-04</b>	0.061	0.196	0.007	0.640	-0.023	0.038	0.039	0.926	-0.803	0.882		
LDL diameter	153	-0.062	0.024	-0.116	-0.008	0.042	0.116	-0.010	0.094	-0.471	0.505	-1.868	0.927		
HDL diameter	153	-0.120	<b>1.12E-04</b>	-0.179	-0.061	0.008	0.291	-0.007	0.023	0.038	0.855	-0.372	0.448		
<b>Apolipoproteins and lipids</b>															
Triglycerides	153	0.121	<b>0.001</b>	0.054	0.187	0.010	0.455	-0.016	0.036	-0.288	0.426	-1.003	0.427		
Total phosphoglyceride	146	-0.008	0.826	-0.081	0.065	-0.006	0.713	-0.039	0.027	0.059	0.897	-0.839	0.956		
Phosphatidylcholines	146	-0.009	0.800	-0.080	0.062	-0.011	0.496	-0.044	0.021	0.293	0.514	-0.596	1.183		
Sphingomyelins	146	-0.030	0.353	-0.094	0.034	-0.026	0.115	-0.059	0.007	0.840	0.066	-0.057	1.736		
Apolipoprotein A-I	153	-0.065	0.049	-0.131	0.000	-0.022	0.124	-0.050	0.006	0.462	0.238	-0.311	1.236		
Apolipoprotein B	153	0.081	0.015	0.016	0.145	-0.010	0.384	-0.034	0.013	0.468	0.154	-0.179	1.114		

Supplementary Table S4 (continued) | Interaction between SLM and BMI

	N	BMI				SLM x BMI				SLM			
		B	p-value*	95% CI		B	p-value*	95% CI		B	p-value*	95% CI	
<b>Glycolysis related metabolites</b>													
Glucose	153	0.031	0.146	-0.011	0.074	0.031	0.339	-0.033	0.096	-0.174	0.849	-1.983	1.634
Lactate	153	0.085	<b>0.001</b>	0.034	0.135	-0.058	0.179	-0.144	0.027	1.081	0.359	-1.248	3.410
Pyruvate	151	0.057	0.082	-0.007	0.121	-0.027	0.425	-0.094	0.040	0.763	0.398	-1.022	2.547
Citrate	153	0.045	0.141	-0.015	0.104	-0.021	0.573	-0.095	0.053	0.492	0.630	-1.533	2.517
Glycerol	151	0.065	<b>4.77E-04</b>	0.029	0.100	0.020	0.453	-0.033	0.073	-1.551	0.038	-3.013	-0.089
<b>Amino acids</b>													
Alanine	151	0.027	0.383	-0.034	0.088	-0.053	0.056	-0.107	0.001	1.992	0.007	0.557	3.428
Glutamine	151	-0.044	0.176	-0.108	0.020	-0.028	0.362	-0.089	0.033	1.164	0.161	-0.472	2.800
Glycine	135	-0.036	0.224	-0.094	0.022	-0.007	0.812	-0.064	0.050	-0.285	0.719	-1.849	1.280
Histidine	153	-0.011	0.680	-0.065	0.043	-0.031	0.441	-0.110	0.048	0.561	0.613	-1.631	2.753
Isoleucine	150	0.064	0.040	0.003	0.126	-0.026	0.319	-0.077	0.025	1.549	0.030	0.151	2.946
Leucine	152	0.047	0.050	0.000	0.095	-0.023	0.356	-0.073	0.026	1.769	0.011	0.423	3.116
Valine	151	0.030	0.349	-0.034	0.094	-0.022	0.449	-0.079	0.035	1.097	0.168	-0.469	2.664
Phenylalanine	153	0.081	0.013	0.018	0.145	-0.028	0.424	-0.099	0.042	0.212	0.826	-1.698	2.122
Tyrosine	153	0.071	0.021	0.011	0.131	-0.023	0.548	-0.097	0.052	0.445	0.674	-1.648	2.538
<b>Ketone bodies</b>													
Acetate	153	0.027	0.561	-0.064	0.118	-0.025	0.305	-0.074	0.023	0.226	0.736	-1.099	1.550
Acetoacetate	153	0.011	0.717	-0.050	0.072	0.020	0.527	-0.042	0.081	-1.239	0.141	-2.896	0.419
3-hydroxybutyrate	151	0.064	0.024	0.009	0.119	-0.029	0.184	-0.072	0.014	1.001	0.098	-0.187	2.189
<b>Fluid balance</b>													
Creatinine	152	-0.019	0.546	-0.082	0.044	-0.004	0.858	-0.044	0.037	-0.296	0.608	-1.436	0.844
Albumin	153	-0.002	0.946	-0.060	0.056	-0.039	0.288	-0.110	0.033	0.743	0.449	-1.195	2.681
<b>Inflammation markers</b>													
Glycoprotein acetyls	153	0.116	<b>0.001</b>	0.050	0.182	0.000	0.997	-0.041	0.041	0.387	0.490	-0.722	1.496

Used model: Metabolite =  $\beta_0 + \beta_1 * \text{BMI} + \beta_2 * (\text{SLMxBMI}) + \beta_3 * \text{SLM} + \beta_4 * \text{Age} + \beta_5 * \text{Gender} + \beta_6 * \text{Status} + \beta_7 * \text{Lipid lowering medication} + \beta_8 * \text{Antihypertensive medication} + u_1 * \text{Household} + \epsilon$

BMI reports  $\beta_1$ , SLM x BMI reports  $\beta_2$ ; SLM reports  $\beta_3$

\* Bold p-values indicate significant associations after FDR correction. † % of total fatty acids

SLM, standardized liquid meal; Double bonds/fatty acids, the number of double bonds in fatty acids. VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

**Supplementary Table S5** | Effect size of the association between diastolic blood pressure and metabolites before and after the standardized liquid meal

	N	B	fasting			postprandial		
			p-value*	95% CI	B	p-value*	95% CI	
<b>Fatty acids</b>								
Total fatty acids	147	0.028	0.005	0.009	0.048	0.026	0.003	0.009
Fatty acid chain length	147	-0.002	0.857	-0.019	0.016	0.001	0.948	-0.026
Double bonds / fatty acids	147	-0.030	<b>0.001</b>	-0.047	-0.013	-0.034	0.007	-0.058
Docosahexaenoic acid	147	-0.013	0.316	-0.038	0.012	-0.015	0.245	-0.039
Linoleic acid	147	0.027	0.002	0.010	0.045	0.025	0.003	0.009
Omega-3 fatty acids	147	-0.002	0.879	-0.026	0.022	-0.004	0.734	-0.026
Omega-6 fatty acids	147	0.023	0.016	0.004	0.042	0.021	0.014	0.004
Polyunsaturated fatty acids	147	0.021	0.036	0.001	0.040	0.019	0.036	0.001
Monounsaturated fatty acids	147	0.029	0.003	0.010	0.048	0.030	0.001	0.013
Saturated fatty acids	147	0.027	0.005	0.008	0.046	0.023	0.025	0.003
<b>Fatty acids, relative to total fatty acids</b>								
Omega-3 fatty acids (%) <sup>†</sup>	147	-0.027	0.019	-0.049	-0.005	-0.028	0.023	-0.052
Omega-6 fatty acids (%) <sup>†</sup>	147	-0.013	0.134	-0.031	0.004	-0.013	0.173	-0.032
Polyunsaturated fatty acids (%) <sup>†</sup>	147	-0.020	0.021	-0.036	-0.003	-0.020	0.060	-0.040
Monounsaturated fatty acids (%) <sup>†</sup>	147	0.019	0.029	0.002	0.037	0.023	0.020	0.004
Saturated fatty acids (%) <sup>†</sup>	147	0.002	0.833	-0.015	0.019	-0.006	0.676	-0.037
<b>Cholesterol</b>								
Total cholesterol	154	0.017	0.062	-0.001	0.036	0.014	0.085	-0.002
non HDL cholesterol	154	0.021	0.019	0.004	0.039	0.017	0.035	0.001
VLDL cholesterol	154	0.024	0.010	0.006	0.043	0.019	0.016	0.004
IDL cholesterol	154	0.017	0.057	-0.001	0.034	0.014	0.070	-0.001
LDL cholesterol	154	0.018	0.042	0.001	0.035	0.013	0.101	-0.003
HDL cholesterol	154	-0.008	0.421	-0.027	0.011	-0.007	0.478	-0.027
Cholesterol esterification	147	0.018	0.052	0.000	0.037	0.015	0.060	-0.001

**Supplementary Table S5 (continued)** | Effect size of the association between diastolic blood pressure and metabolites before and after the standardized liquid meal

	N	B	fasting			postprandial		
			p-value*	95% CI	B	p-value*	95% CI	
<b>Lipoprotein lipid concentration</b>								
Extremely large VLDL	150	0.025	0.008	0.007	0.043	0.034	0.006	0.010
Very large VLDL	149	0.026	0.010	0.006	0.046	0.030	0.009	0.008
Large VLDL	151	0.027	0.015	0.005	0.048	0.026	0.009	0.007
Medium VLDL	154	0.028	0.006	0.008	0.047	0.023	0.005	0.007
Small VLDL	154	0.024	0.013	0.005	0.043	0.018	0.022	0.003
Very small VLDL	154	0.018	0.063	-0.001	0.037	0.013	0.082	-0.002
IDL	154	0.017	0.064	-0.001	0.035	0.014	0.074	-0.001
Large LDL	154	0.018	0.046	0.000	0.036	0.015	0.073	-0.001
Medium LDL	154	0.019	0.037	0.001	0.036	0.014	0.089	-0.002
Small LDL	154	0.018	0.042	0.001	0.036	0.015	0.089	-0.002
Very large HDL	154	-0.011	0.233	-0.030	0.007	-0.007	0.398	-0.022
Large HDL	149	-0.007	0.389	-0.025	0.010	-0.006	0.493	-0.023
Medium HDL	154	0.005	0.632	-0.015	0.024	0.009	0.449	-0.014
Small HDL	154	0.012	0.205	-0.006	0.030	0.008	0.445	-0.013
<b>Lipoprotein particle size</b>								
VLDL diameter	154	0.026	0.009	0.006	0.045	0.024	0.005	0.007
LDL diameter	154	-0.007	0.471	-0.025	0.012	-0.004	0.642	-0.023
HDL diameter	154	-0.011	0.203	-0.028	0.006	-0.008	0.341	-0.025
<b>Apolipoproteins and lipids</b>								
Triglycerides	154	0.027	0.007	0.008	0.046	0.025	0.005	0.008
Total phosphoglyceride	147	0.018	0.054	0.000	0.037	0.015	0.082	-0.002
Phosphatidylcholines	147	0.019	0.050	0.000	0.038	0.016	0.073	-0.002
Sphingomyelins	147	0.006	0.500	-0.012	0.025	0.002	0.850	-0.016
Apolipoprotein A-I	154	0.002	0.823	-0.016	0.020	0.003	0.741	-0.016
Apolipoprotein B	154	0.024	0.013	0.005	0.043	0.020	0.015	0.004

**Supplementary Table S5 (continued)** | Effect size of the association between diastolic blood pressure and metabolites before and after the standardized liquid meal

	N	B	fasting			postprandial		
			p-value*	95% CI	B	p-value*	95% CI	
<b>Glycolysis related metabolites</b>								
Glucose	154	0.011	0.051	0.000	0.022	0.017	0.117	-0.004
Lactate	154	0.017	0.045	0.000	0.034	0.011	0.342	-0.012
Pyruvate	152	0.003	0.786	-0.017	0.022	0.015	0.161	-0.006
Citrate	154	0.020	0.043	0.001	0.039	0.017	0.148	-0.006
Glycerol	152	0.007	0.149	-0.003	0.017	0.019	0.047	0.000
<b>Amino acids</b>								
Alanine	152	0.006	0.494	-0.011	0.023	0.005	0.594	-0.015
Glutamine	152	0.008	0.429	-0.012	0.029	0.010	0.348	-0.011
Glycine	136	-0.017	0.037	-0.033	-0.001	-0.014	0.162	-0.034
Histidine	154	0.006	0.511	-0.012	0.024	0.002	0.806	-0.017
Isoleucine	151	0.012	0.238	-0.008	0.031	0.009	0.313	-0.008
Leucine	153	0.006	0.465	-0.010	0.021	0.007	0.418	-0.010
Valine	152	0.001	0.954	-0.021	0.022	0.003	0.818	-0.020
Phenylalanine	154	0.004	0.721	-0.017	0.025	0.001	0.947	-0.022
Tyrosine	154	0.009	0.393	-0.012	0.030	0.009	0.412	-0.012
<b>Ketone bodies</b>								
Acetate	154	0.020	0.217	-0.012	0.052	0.023	0.069	-0.002
Acetoacetate	154	0.009	0.369	-0.010	0.028	0.005	0.658	-0.016
3-hydroxybutyrate	152	0.012	0.243	-0.008	0.032	0.006	0.553	-0.014
<b>Fluid balance</b>								
Creatinine	153	0.008	0.409	-0.011	0.028	0.006	0.584	-0.015
Albumin	154	0.007	0.460	-0.012	0.026	0.009	0.481	-0.016
<b>Inflammation markers</b>								
Glycoprotein acetyls	154	0.019	0.071	-0.002	0.040	0.022	0.039	0.001

Effect sizes indicate the association magnitudes in units of 1-SD metabolite concentration per 1-mmHg increment in diastolic blood pressure.

\* Bold p-values indicate significant associations after FDR correction. <sup>†</sup> % of total fatty acids

Double bonds/fatty acids: the number of double bonds in fatty acids. VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

**Supplementary Table S6** | Effect size of the association between insulin and metabolites before and after the standardized liquid meal

	N	B	fasting			postprandial		
			p-value*	95% CI	B	p-value*	95% CI	
<b>Fatty acids</b>								
Total fatty acids	148	0.043	0.053	0.000	0.086	0.005	0.106	-0.001
Fatty acid chain length	148	0.011	0.351	-0.013	0.036	0.007	0.044	0.000
Double bonds / fatty acids	148	-0.039	0.047	-0.078	-0.001	-0.008	<b>0.015</b>	-0.014
Docosahexaenoic acid	148	0.014	0.432	-0.021	0.048	0.003	0.407	-0.004
Linoleic acid	148	0.028	0.105	-0.006	0.062	0.003	0.387	-0.004
Omega-3 fatty acids	148	0.017	0.355	-0.019	0.052	0.003	0.432	-0.004
Omega-6 fatty acids	148	0.026	0.155	-0.010	0.062	0.002	0.579	-0.005
Polyunsaturated fatty acids	148	0.026	0.153	-0.010	0.062	0.002	0.544	-0.005
Monounsaturated fatty acids	148	0.050	0.036	0.003	0.096	0.006	0.050	0.000
Saturated fatty acids	148	0.040	0.051	0.000	0.081	0.006	0.071	-0.001
<b>Fatty acids, relative to total fatty acids</b>								
Omega-3 fatty acids (%) <sup>†</sup>	148	-0.017	0.402	-0.058	0.023	-0.001	0.678	-0.008
Omega-6 fatty acids (%) <sup>†</sup>	148	-0.038	0.028	-0.071	-0.004	-0.008	<b>0.005</b>	-0.013
Polyunsaturated fatty acids (%) <sup>†</sup>	148	-0.040	0.035	-0.078	-0.003	-0.008	<b>0.009</b>	-0.013
Monounsaturated fatty acids (%) <sup>†</sup>	148	0.040	0.054	-0.001	0.080	0.005	0.091	-0.001
Saturated fatty acids (%) <sup>†</sup>	148	-0.001	0.946	-0.026	0.024	0.003	0.397	-0.004
<b>Cholesterol</b>								
Total cholesterol	155	0.008	0.622	-0.024	0.040	0.000	0.918	-0.006
non HDL cholesterol	155	0.033	0.048	0.000	0.066	0.002	0.502	-0.005
VLDL cholesterol	155	0.058	<b>0.004</b>	0.019	0.096	0.004	0.124	-0.001
IDL cholesterol	155	0.014	0.393	-0.018	0.045	0.000	0.933	-0.007
LDL cholesterol	155	0.022	0.163	-0.009	0.052	0.001	0.700	-0.006
HDL cholesterol	155	-0.070	<b>0.001</b>	-0.111	-0.030	-0.007	<b>0.002</b>	-0.012
Cholesterol esterification	148	0.009	0.571	-0.024	0.043	0.001	0.829	-0.006

**Supplementary Table S6 (continued)** | Effect size of the association between insulin and metabolites before and after the standardized liquid meal

	N	B	fasting			postprandial		
			p-value*	95% CI	B	p-value*	95% CI	
<b>Lipoprotein lipid concentration</b>								
Extremely large VLDL	151	0.064	<b>0.014</b>	0.013	0.114	0.009	<b>0.008</b>	0.002
Very large VLDL	150	0.073	<b>0.018</b>	0.013	0.133	0.009	<b>0.003</b>	0.003
Large VLDL	152	0.083	<b>0.006</b>	0.025	0.142	0.009	<b>0.001</b>	0.004
Medium VLDL	155	0.081	<b>1.36E-04</b>	0.040	0.121	0.008	<b>0.002</b>	0.003
Small VLDL	155	0.065	<b>0.001</b>	0.026	0.104	0.006	0.040	0.000
Very small VLDL	155	0.034	0.051	0.000	0.068	0.002	0.538	-0.004
IDL	155	0.016	0.324	-0.016	0.049	0.000	0.900	-0.007
Large LDL	155	0.021	0.210	-0.012	0.053	0.001	0.751	-0.006
Medium LDL	155	0.027	0.088	-0.004	0.058	0.002	0.572	-0.005
Small LDL	155	0.026	0.094	-0.005	0.057	0.003	0.448	-0.004
Very large HDL	155	-0.063	<b>4.20E-04</b>	-0.097	-0.029	-0.005	<b>0.010</b>	-0.010
Large HDL	150	-0.059	<b>0.001</b>	-0.094	-0.025	-0.006	<b>0.014</b>	-0.011
Medium HDL	155	-0.038	<b>0.020</b>	-0.069	-0.006	-0.004	0.027	-0.008
Small HDL	155	0.012	0.415	-0.017	0.041	0.001	0.635	-0.003
<b>Lipoprotein particle size</b>								
VLDL diameter	155	0.082	<b>2.33E-04</b>	0.040	0.125	0.009	<b>7.45E-05</b>	0.005
LDL diameter	155	-0.027	0.046	-0.053	-0.001	-0.006	0.018	-0.010
HDL diameter	155	-0.074	<b>4.78E-05</b>	-0.109	-0.040	-0.008	<b>4.23E-04</b>	-0.012
<b>Apolipoproteins and lipids</b>								
Triglycerides	155	0.074	<b>0.001</b>	0.032	0.116	0.008	<b>0.003</b>	0.003
Total phosphoglyceride	148	-0.004	0.804	-0.038	0.030	-0.001	0.688	-0.006
Phosphatidylcholines	148	-0.005	0.771	-0.037	0.027	-0.001	0.641	-0.006
Sphingomyelins	148	0.007	0.696	-0.026	0.039	-0.001	0.770	-0.008
Apolipoprotein A-I	155	-0.048	<b>0.004</b>	-0.080	-0.015	-0.004	0.040	-0.009
Apolipoprotein B	155	0.049	<b>0.013</b>	0.011	0.088	0.004	0.204	-0.002

**Supplementary Table S6 (continued)** | Effect size of the association between insulin and metabolites before and after the standardized liquid meal

	N	B	fasting			postprandial		
			p-value*	95% CI	B	p-value*	95% CI	
<b>Glycolysis related metabolites</b>								
Glucose	155	0.029	<b>0.005</b>	0.009	0.049	0.006	0.049	0.000
Lactate	155	0.049	<b>2.46E-05</b>	0.027	0.072	0.008	<b>0.007</b>	0.002
Pyruvate	153	0.048	<b>0.005</b>	0.015	0.080	0.005	0.151	-0.002
Citrate	155	0.041	<b>0.016</b>	0.008	0.073	0.007	<b>0.003</b>	0.003
Glycerol	153	0.028	<b>0.001</b>	0.011	0.045	0.006	<b>0.001</b>	0.003
<b>Amino acids</b>								
Alanine	153	0.025	0.075	-0.003	0.052	0.007	<b>0.006</b>	0.002
Glutamine	153	-0.022	0.219	-0.057	0.013	-0.004	0.213	-0.011
Glycine	137	-0.024	0.063	-0.049	0.001	-0.003	0.297	-0.008
Histidine	155	0.018	0.251	-0.013	0.049	-0.001	0.672	-0.007
Isoleucine	152	0.079	<b>6.91E-06</b>	0.046	0.112	0.009	<b>2.73E-06</b>	0.006
Leucine	154	0.049	<b>3.38E-05</b>	0.027	0.071	0.008	<b>1.87E-05</b>	0.004
Valine	153	0.060	<b>2.41E-06</b>	0.036	0.084	0.005	0.039	0.000
Phenylalanine	155	0.065	<b>9.19E-06</b>	0.037	0.093	0.009	<b>0.001</b>	0.004
Tyrosine	155	0.060	<b>4.06E-06</b>	0.035	0.084	0.009	<b>3.69E-04</b>	0.004
<b>Ketone bodies</b>								
Acetate	155	0.008	0.671	-0.031	0.048	-0.001	0.496	-0.005
Acetoacetate	155	0.013	0.400	-0.018	0.045	-0.004	0.136	-0.009
3-hydroxybutyrate	153	0.054	<b>0.001</b>	0.023	0.086	0.006	<b>0.008</b>	0.002
<b>Fluid balance</b>								
Creatinine	154	0.019	0.132	-0.006	0.043	0.001	0.453	-0.002
Albumin	155	0.011	0.411	-0.016	0.038	-0.001	0.767	-0.008
<b>Inflammation markers</b>								
Glycoprotein acetyls	155	0.088	<b>2.04E-04</b>	0.043	0.133	0.007	0.057	0.000

Effect sizes indicate the association magnitudes in units of 1-SD metabolite concentration per 1-MU/L increment in insulin.

\* Bold p-values indicate significant associations after FDR correction. † % of total fatty acids

Double bonds/fatty acids: the number of double bonds in fatty acids. VLDL, very low density lipoprotein; IDL, intermediate density lipoprotein; LDL, low density lipoprotein; HDL, high density lipoprotein.

**Supplementary Table S7 | Nutritional content Nutridrink**

per 100 ml:

<b>Energy</b>	150/625	<b>kcal/kJ</b>	<b>Trace elements</b>		
<b>Fat (35 En%)</b>	5.8	<b>g</b>	Iron	2.4	<b>mg</b>
Saturated fat	0.6	<b>g</b>	Zinc	1.8	<b>mg</b>
Monounsaturated fat	3.5	<b>g</b>	Copper	0.27	<b>mg</b>
Polyunsaturated fat	1.7	<b>g</b>	Manganese	0.5	<b>mg</b>
Linoleic acid	1.4	<b>g</b>	Fluorine	0.15	<b>mg</b>
α-Linolenic acid	0.27	<b>g</b>	Molybdenum	15	<b>μg</b>
Arachidonic acid	-	<b>mg</b>	Selenium	8.6	<b>μg</b>
Docosahexaenoic acid	-	<b>mg</b>	Chromium	10	<b>μg</b>
Eicosapentaenoic acid	-	<b>mg</b>	Iodine	20	<b>μg</b>
<b>Vitamins</b>					
<b>Carbohydrates (49 En%)</b>	18.4	<b>g</b>	A	123	<b>μg-RE</b>
Glucose	0.1	<b>g</b>	Carotenoids	0.3	<b>mg</b>
Fructose	-	<b>g</b>	D	1.1	<b>μg</b>
Lactose	<0.025	<b>g</b>	E	1.9	<b>mg α-TE</b>
Maltose	0.6	<b>g</b>	K	8	<b>μg</b>
Sacharose	6	<b>g</b>	Thiamine	0.23	<b>mg</b>
Polysacharose	11.3	<b>g</b>	Riboflavin	0.24	<b>mg</b>
Others	0.4	<b>g</b>	Niacin	2.7	<b>mg NE</b>
			Pantothenic acid	0.8	<b>mg</b>
<b>Fibers</b>	-	<b>g</b>	<b>Others</b>		
<b>Protein (16 En%)</b>	5.9	<b>g</b>	Carnitine	-	<b>mg</b>
Casein	5.9	<b>g</b>	Choline	55	<b>mg</b>
Whey protein	-	<b>g</b>	Taurine	-	<b>mg</b>
<b>Salt</b>	0.23	<b>g</b>	<b>Osmolarity</b>		
<b>Liquids</b>	78	<b>ml</b>	455 mOsmol/l		
<b>Minerals</b>					
Sodium	90	<b>mg</b>			
Potassium	159	<b>mg</b>			
Chlorine	87	<b>mg</b>			
Calcium	91	<b>mg</b>			
Phosphorus	78	<b>mg</b>			
Magnesium	23	<b>mg</b>			

**Supplementary Table S8 | Nutritional content amino acids Nutridrink**

per 100 ml:

L-Alanine	193 mg
L-Arginine	227 mg
L-Asparagine zuur / L-Asparagine	446 mg
L-Cystine	20.8 mg
L-Glutaminezuur / L-Glutamine	1,394 mg
Glycine	115 mg
L-Histidine	186 mg
L-Isoleucine	338 mg
L-Leucine	606 mg
L-Lysine	545 mg
L-Methionine	183 mg
L-Fenylalanine	323 mg
L-Proline	600 mg
L-Serine	381 mg
L-Threonine	279 mg
L-Tryptofaan	82.2 mg
L-Tyrosine	349 mg
L-Valine	432 mg
L-Methione + L-Cystine	204 mg
L-Phenylalanine + L-Tyrosine	673 mg

## References

- <sup>1</sup> Würtz, P. *et al.* Metabolic signatures of adiposity in young adults: Mendelian randomization analysis and effects of weight change. *PLoS. Med.* 11. e1001765 (2014).